Remarks

The Final Office Action mailed October 30, 2002 has been received and reviewed. Claims 12-15 having been canceled, and claim 26 having been amended, the pending claims are claims 1, 3-11, 23 and 26.

Claim 26 has been amended to correct an obvious typographical error.

Reconsideration and withdrawal of the rejections are respectfully requested.

Applicants' Invention

Applicants' presently disclosed invention relates to a method of transferring molecules positioned within a matrix to a laminate. Notably, the specification (e.g., page 5, lines 15-25) describes a matrix as follows:

> The matrix of the claimed method can be any matrix suitable for separating molecules. Such separation can be based on differences in the size, shape, electrical charge or any other physical or chemical property of the molecules that can be the basis for separating molecules from one another in a mixture. As nonlimiting examples, agarose gels are known to be useful for separating polynucleotides and polyacrylamide gradient gels containing sodium dodecyl sulfate (SDS) are known to be useful for separating polypeptides, e.g., proteins. The matrix may be of uniform concentration throughout, such as a 1% agarose, which may be used to separate polynucleotides. Alternatively, the matrix may be a gradient, such as a 4-15% SDS-polyacrylamide gel for the separation of proteins. Other possible types of gels are known and may be used for the claimed method. One of skill in the art will be able to select a matrix appropriate for any desired application.

The method includes: (a) providing a laminate including i) a shrinkable polymeric substrate having a projected surface area and a topographical surface area, and ii) a hydrogel disposed on at least a portion of the substrate, the hydrogel including linking agents; (b) contacting the matrix with the laminate; (c) transferring molecules from the matrix to the

laminate; (d) removing the matrix from the laminate; and (e) shrinking the laminate so that the topographical surface area is greater than the projected surface area.

Rejection under 35 U.S.C. §103

The Examiner rejected claims 1, 3-11, 23, and 26 under 35 U.S.C. §103(a) as allegedly being unpatentable over PCT International Publication No. WO 99/53319 (Halverson et al.) in view of U.S. Pat. No. 4,589,965 (Kreisher et al.). Applicants respectfully traverse the rejection.

"To establish a *prima facie* case of obviousness . . . [f]irst, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success." M.P.E.P. §706.02(j). Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case of obviousness.

Halverson et al. disclose high-density miniaturized arrays and methods of manufacturing high-density miniaturized arrays. The methods of making the arrays include affixing one or more reactants directly to the array substrate by spotting, as exemplified in Example 4 using a capillary tube and in Example 5 using an aluminum post. As acknowledged by the Examiner, Halverson et al. lack specific disclosures of transferring *molecules positioned within a matrix*, contacting *the matrix with the laminate*, transferring molecules *from the matrix to the laminate*, and removing *the matrix from the laminate*.

Kreisher et al. disclose a method of electroblotting molecules from a gel to a blot membrane:

> The electrophoretically resolved material in the gelatin sheet is placed in contacting relationship with an immobilizing material. *Any suitable immobilizing material* can be used, such as membranes, papers, nylon, nitrocellulose, diazobenzyloxymethyl (DBM) paper, diazophenylthioether (DPT) paper, and the like.

(Column 4, lines 5-10, emphasis added). However, Kreisher et al. lack, among other things, a disclosure of (1) a laminate including i) a shrinkable polymeric substrate having a projected surface area and a topographical surface area, and ii) a hydrogel disposed on at least a portion of the substrate, the hydrogel including linking agents, and (2) shrinking the laminate so that the topographical surface area is greater than the projected surface area.

"The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure." M.P.E.P. §706.02(j). Applicants respectfully submit that, absent Applicants' present disclosure, it would *not be obvious* to one of skill in the art that the laminate disclosed by Halverson et al. would be a *suitable immobilizing material* for use in the method of electroblotting disclosed by Kreisher et al.

Membranes and Papers are Suitable Immobilizing Materials for Use in Electroblotting Methods.

Electrophoretic transfer or electroblotting is defined as "a development of the technique of blot transfer, in which proteins or nucleic acids are transferred from a separation gel to nitrocellulose or diethylaminoethyl- (DEAE-)cellulose *membranes* or to diazobenzyloxymethyl- (DBM)- or diazophenylthioether- (DPT-) *paper* by electrophoresis" (EXHIBIT A: Oxford Dictionary of Biochemistry and Molecular Biology, Oxford University Press, 1997, emphasis added).

Consistent with the standard description of an immobilizing material, Kreisher et al. describe *suitable immobilizing materials* as "*membranes*, *papers*, nylon, nitrocellulose, diazobenzyloxymethyl (DBM) *paper*, diazophenylthioether (DPT) *paper*, and the like" (column 4, lines 7-10, emphasis added).

Halverson et al. Fail to Specifically Disclose an Array that is a Membrane or Paper.

Halverson et al. disclose arrays as including a "substrate with a coating of linking

agents" (Abstract). Halverson et al. state that "[t]he substrate of the present invention is a polymeric material" (page 7, line 32). Halverson et al. further state that "[t]he substrate provides a preferably non-porous surface upon which coatings and/or reactants may be affixed" (page 8, lines 34-35). Halverson et al. describe in detail materials that are useful for substrates including polymeric materials (e.g., page 8, lines 9-18), preferred oriented films (e.g., page 8, line 19 to page 9, line 35), and elastomeric materials (e.g., page 10, lines 5-9). However, Halverson et al. fail to specifically disclose an array that is a membrane or paper.

One of Skill in the Art Would Have No Reasonable Expectation of Success in Using an Array of Halverson et al. as an Immobilizing Material in the Electroblotting Method of Kreisher et al.

One of skill in the art might arguably have a reasonable expectation of success in using a *porous* material (e.g., a membrane or paper) as an immobilizing material in the electroblotting method of Kreisher et al. However, Halverson et al. not only fail to specifically disclose an array that is a porous material, they in fact *teach away* from an array that is a porous material by suggesting that the array includes a substrate that provides a preferably *non-porous* surface (e.g., page 8, lines 34-35).

Thus, absent Applicants' present disclosure, one of skill in the art would have no motivation to use an array as disclosed by Halverson et al. as an immobilizing material in the electroblotting method of Kreisher et al., with a reasonable expectation of success.

In light of the remarks presented herein above, Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case of obviousness. Applicants respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. §103.

Summary

It is respectfully submitted that all the pending claims are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

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CERTIFICATE UNDER 37 CFR §1.8:
The undersigned hereby certifies that this paper is being transmitted by facsimile in accordance with 37 CFR §1.6(d) to the Patent and Trademark Office, addressed to Assistant Commissioner for Patents, Attn: BOX AF, Washington, D.C. 20231, on this 29 day of January, 2003, at 3:38 p.m. (Central Time).

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Name: Rachel Cylkowski-Graham

APPENDIX A - SPECIFICATION/CLAIM AMENDMENTS INCLUDING NOTATIONS TO INDICATE CHANGES MADE
Serial No.: 09/819,317
Docket No.: 56066US002

Amendments to the following are indicated by underlining what has been added and bracketing what has been deleted. Additionally, all amendments have been marked in bold typeface.

In the Claims

For convenience, all pending claims are shown below.

1. A method of transferring molecules positioned within a matrix to a laminate comprising:

(a) providing a laminate comprising

i) a shrinkable polymeric substrate having a projected surface area and a topographical surface area, and

ii) a hydrogel disposed on at least a portion of the substrate, the hydrogel comprising linking agents;

(b) contacting the matrix with the laminate;

(c) transferring molecules from the matrix to the laminate;

(d) removing the matrix from the laminate; and

(e) shrinking the laminate so that the topographical surface area is greater than the projected surface area.

3. The method of claim 1 wherein the linking agents comprise azlactone copolymers.

4. The method of claim 1 wherein the laminate further comprises a mask layer.

5. The method of claim 4 wherein the mask layer is in direct contact with the substrate and underlies the hydrogel.

6. The method of claim 1 wherein the one or more molecules are transferred from the matrix to the laminate by electroblotting.

7. The method of claim 1 wherein the matrix contains polynucleotides, polypeptides, polysaccharides, or combinations thereof.

8. The method of claim 1 wherein the matrix comprises an agarose gel or a polyacrylamide gel.

9. The method of claim 1 further comprising detecting the one or more molecules transferred from the matrix to the laminate.

10. The method of claim 1 wherein the shrinkable polymeric film is flexible.

11. The method of claim 1 wherein the shrinkable polymeric film is heat-shrinkable.

23. The method of claim 1 wherein the molecules comprise polynucleotides, polypeptides, polysaccharides, or combinations thereof.

26. **(Amended)** The method of claim 1 wherein the step of transferring molecules from the matrix to the laminate comprises forming **[covalently]**__**covalent**__ bonds between at least a portion of the molecules and the linking agents.

Exhibit A

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electronvolt *or* **electron volt** *symbol*: eV; a non-SI unit of energy equal to the kinetic energy acquired by an electron when accelerated through an electric potential difference of 1 volt. $1\ eV = e \times V \approx 1.602\ 18 \times 10^{-19}$ J, where e is the **elementary charge** and V is the volt.

electroosmosis *or (formerly)* **electroendosmosis** the motion of a liquid through a membrane (or plug or capillary) consequent upon the application of an electric field across the membrane. A similar phenomenon may occur in electrophoresis, where many of the supporting media used, e.g. paper or agar, acquire negative charges during electrophoresis at alkaline pHs and, since the medium cannot move, H_3O^+ ions move towards the cathode, giving the effect of an osmotic movement of solvent towards the cathode and making electrically neutral molecules appear to be cationic. —**electroosmotic** *adj.*

electropherogram *a variant spelling of* **electrophoretogram**.

electrophile *or* **electrophilic reagent** any chemical species that is preferentially attracted to a region of high electron density in another species during a chemical reaction. Such reagents normally are positively charged or contain electron-deficient chemical groups. They tend to react with electron-rich or negatively charged chemical species. *Compare* **nucleophile**.

electrophilic 1 of, pertaining to, or being an **electrophile**; having or involving an affinity for regions of high electron density in a chemical reactant. 2 describing a chemical reaction in which an electrophile participates.

electrophilic catalysis catalysis by a Lewis acid, i.e. any chemical species that abstracts an electron pair from the reactant.

electrophilic displacement *an alternative term for* **electrophilic substitution reaction**.

electrophilicity the relative reactivity of an **electrophile**, measured by the relative rate constants of different electrophiles towards a common reactant.

electrophilic reagent *an alternative name for* **electrophile**.

electrophilic substitution reaction *or* **electrophilic displacement** a chemical reaction in which an **electrophile** effects heterolytic substitution in another reactant, both bonding electrons being supplied by that other reactant.

electrophoresis 1 the phenomenon of the movement of ions (including macromolecular ions) or charged particles or ions through a fluid under the influence of an electric field applied to the fluid. A number of different media have been used as the fluid support, including paper, cellulose acetate, starch gel, and polycrylamide gel. Ions or particles bearing a net positive charge tend to move towards the negative pole of the electric field and vice versa, the rate of movement of a particular variety of ion or particle depending, *inter alia*, on its charge-to-mass ratio. The phenomenon has been widely applied in separating proteins, nucleic acids, and other charged molecular species for analytical or preparative purposes, and also in the analytical or preparative fractionation of heterogeneous populations of dispersed cells or other types of macroscopic particles. 2 the act or process of causing ions or charged particles so to migrate; any technique based upon such a phenomenon, e.g. **continuous flow electrophoresis**, **immunoelectrophoresis**, **moving boundary electrophoresis**, **paper electrophoresis**, **polycrylamide gel electrophoresis**, **zone electrophoresis**. *See also* **electrodecantation**. —**electrophoretic** *adj.*

electrophoresis convection *an alternative term for* **electrodecantation**.

electrophoretic effect the phenomenon of decreased **electrophoretic mobility** of a charged macromolecule caused by the movement of counter ions and/or solvent molecules in the opposite direction to that of the macromolecule.

electrophoretic mobility *symbol*: u; the **electrophoretic velocity**, v, of a charged particle expressed per unit field strength; hence, $u = v/E$, where E is the field strength. The value of u is positive if the particle moves towards the pole of lower potential and negative in the opposite case. The electrophoretic mobility depends only on molecular parameters.

electrophoretic molecular sieving *(sometimes) an alternative term for* **polyacrylamide (gel) electrophoresis**.

electrophoretic titration curve the pH-mobility curve of an ampholyte, e.g. a protein, generated by subjecting a zone of it to electrophoresis in a gel slab at right angles to a preformed, stationary pH gradient. *Compare* **isoelectric focusing**.

electrophoretic transfer *or* **electroblotting** a development of the technique of blot transfer, in which proteins or nucleic acids are transferred from a separation gel to nitrocellulose or diethylaminoethyl- (DEAE-)cellulose membranes or to diazobenzyloxymethyl- (DBM)- or diazophenylthioether- (DPT-) paper by electrophoresis, rather than by capillary flow, with a consequent decrease in the time required for the transfer. The membrane or paper bearing a resultant pattern of separated substances has been termed an **electroblot**. *See* **blotting**.

electrophoretic velocity *symbol*: v; the velocity of a charged particle during electrophoresis. It is normally proportional to the electric field strength. *Compare* **electrophoretic mobility**.

electrophoretogram *or* **electropherogram** the result of a zone-electrophoretic separation, either directly visible or after staining or processing to produce a graph.

electrophysiology the part of physiology concerned with the electrical phenomena associated with bodily processes, such as nervous and muscular activity.

electroporate to create momentary pores in the membranes of living cells, without loss of their viability, by exposing them to a sequence of brief electrical pulses of high field strength. The reversible breakdown of the cell membranes thus caused enables treated cells to take up exogenous material (e.g. drugs or foreign DNA). —**electroporated** *adj.*; **electroporation** *n.*

electroporator an apparatus or device for effecting electroporation.

electropositive 1 describing an atom or group of atoms that tends to give up electrons, especially in the formation of a covalent bond. 2 describing any chemical or other entity that carries a positive charge and hence tends to move to the cathode in **electrophoresis**.

electropositivity a measure of the power of an atom or group of atoms to give up electrons to other parts of the same molecular entity.

electrospray a technique used in **mass spectrometry** in which a dilute acidic solution of the macromolecule is sprayed from a metal syringe needle maintained at +5000 V, forming fine highly charged droplets from which the solvent rapidly evaporates.

electrostatic of or pertaining to static electricity or electrostatics.

electrostatic bond any valency linkage between atoms arising from the transfer of one or more outer-shell electrons of one atom to the outer shell of another atom, leading to more complete outer shells in both atoms. The dissociation of an electrostatic bond leads to the production of ions.

electrostatic field any **electric field** produced by stationary charges.

electrostatic interaction any of the attractive or repulsive forces between atoms and/or groups of atoms and/or molecules that are due to the presence of ionized chemical entities and to the electronegative and electropositive properties of these atoms, groups, or molecules. *Compare* **electric field**.

electrostatic precipitation the removal of small particles suspended in a gas by electrostatic charging followed by precipitation onto a highly charged collector.

electrostatics the branch of physics concerned with static electricity.

electrostatic units *abbr*: esu *or* ESU; a system of electrical units, used in the cgs system, based upon the electrostatic unit of electric charge, i.e. the quantity of electricity that will repel an equal quantity of electricity, 1 cm distant from it in a vacuum, with the force of 1 dyne.

electrostriction the reversible change in dimensions of a dielectric when an electric field is applied to it. For example, the